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1994  
a/m/03

--This is a continuation of co-pending application Serial No. 08/233,002, filed April 25,

*now U.S. Patent 5,747,469, which*

### In the Claims

Please amend claims 1-45 as follows:

1. (Amended) The method of claim 1, wherein said cell is contacted with a recombinant, non-viral vector that expresses a p53 protein in said cell in combination with a DNA damaging agent.

Do not  
initials  
X, a, a  
2  
2. (Amended) The method of claim 4, wherein said p53-expressing recombinant, non-viral vector is a naked DNA plasmid[,] or a plasmid within a liposome[, a retroviral vector, an AAV vector, or a recombinant adenoviral vector].

Al 3  
7. (Amended) The method of claim [6]4, wherein said p53-expressing recombinant, non-viral vector [is a recombinant adenoviral vector comprising] comprises a p53 expression region positioned under the control of [the cytomegalovirus IE] a promoter.

8. (Amended) The method of claim [6]4, wherein said recombinant, non-viral [adenoviral] vector comprises a p53 expression region, the cytomegalovirus IE promoter and the SV40 early polyadenylation signal.

Al 4  
21. (Amended) The method of claim 1, wherein said cell is a [human] tumor cell.

*AS*  
26. (Amended) The method of claim [1]21, wherein said cell is located within an animal at a tumor site and said p53 protein or gene and DNA damaging agent are administered to the animal in a pharmacologically acceptable form.

*Q6*  
28. (Amended) The method of claim 27, comprising injecting into a tumor site a therapeutically effective amount of a pharmaceutical composition comprising a [recombinant adenovirus containing a] recombinant vector that expresses p53 in [the]a tumor cell, and contacting the tumor with a DNA damaging agent.

*Q1*  
*36*<sup>29</sup>. (Amended) The composition of claim 35, wherein said recombinant vector is a naked DNA plasmid[,] or a plasmid within a liposome[, a retroviral vector, an AAV vector, or a recombinant adenoviral vector].

Please add the following new claims:

*Q8*  
--46. The method of claim 21, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with X-ray radiation, UV-irradiation,  $\gamma$ -irradiation or microwaves.

*SUB*  
47. The method of claim 46, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with X-ray radiation.

*F9/*  
48. The method of claim 46, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with UV-irradiation.

49. The method of claim 46, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with  $\gamma$ -irradiation.

*A8C0X*

50. The method of claim 46, wherein the tumor cell is contacted with a DNA damaging agent by irradiating the tumor cell with microwaves.

*Sub P9,  
cont'd*

51. The method of claim 21, wherein the tumor cell is contacted with a pharmaceutical composition comprising a DNA damaging compound.

52. The method of claim 51, wherein the DNA damaging agent is cisplatin.

*Sub B7*

53. The method of claim 51, wherein the DNA damaging agent is doxorubicin.

*Sub B7*

54. The method of claim 51, wherein the DNA damaging agent is etoposide.

55. The method of claim 51, wherein the DNA damaging agent is verapamil.

56. The method of claim 51, wherein the DNA damaging agent is podophyllotoxin.

57. The method of claim 51, wherein the DNA damaging agent is 5-FU.

58. The method of claim 51, wherein the DNA damaging agent is actinomycin-D.

Q8 cont:

59. The method of claim 51, wherein the DNA damaging agent is adriamycin.

Sub B1  
cont'd

60. The method of claim 51, wherein the DNA damaging agent is camptothecin.

61. The method of claim 51, wherein the DNA damaging agent is mitomycin C.

62. The method of claim 27, wherein a tumor site is contacted with a DNA damaging agent by irradiating the tumor site with X-ray radiation.

63. The method of claim 27, wherein a tumor site is contacted with a DNA damaging agent by irradiating the tumor site with UV-irradiation.

64. The method of claim 27, wherein a tumor site is contacted with a DNA damaging agent by irradiating the tumor site with  $\gamma$ -irradiation.

65. The method of claim 27, wherein a tumor site is contacted with a DNA damaging agent by irradiating the tumor site with microwaves.

66. The method of claim 21, wherein the tumor cell is contacted with a DNA damaging agent by administering to the animal a pharmaceutical composition comprising a DNA damaging compound.

Q8 cont.

67. The method of claim 21, wherein the DNA damaging agent is cisplatin.
68. The method of claim 21, wherein the DNA damaging agent is doxorubicin.
69. The method of claim 21, wherein the DNA damaging agent is etoposide.
70. The method of claim 21, wherein the DNA damaging agent is verapamil.
71. The method of claim 21, wherein the DNA damaging agent is podophyllotoxin.
72. The method of claim 21, wherein the DNA damaging agent is 5-FU.
73. The method of claim 21, wherein the DNA damaging agent is actinomycin-D.
74. The method of claim 21, wherein the DNA damaging agent is adriamycin.
75. The method of claim 21, wherein the DNA damaging agent is camptothecin.
76. The method of claim 21, wherein the DNA damaging agent is mitomycin C.

*A b corp*

77. The method of claim 4, wherein said vector is administered prior to said DNA damaging agent.

*1 v B*  
*B 7*

78. The method of claim 4, wherein said vector is administered after said DNA damaging agent.

79. The method of claim 4, wherein said vector is administered at the same time as said DNA damaging agent.

80. The method of claim 28, wherein said vector is administered prior to said DNA damaging agent.

81. The method of claim 28, wherein said vector is administered after said DNA damaging agent.

82. The method of claim 28, wherein said vector is administered at the same time as said DNA damaging agent.

*1 v B*  
*B 7*

83. The method of claim 28, wherein said vector is delivered endoscopically, intravenously, intratracheally, intralesionally, percutaneously or subcutaneously.

*Acct*

84. The method of claim 28, wherein said tumor site is a resected tumor bed.

85. The method of claim 28, wherein said administration is repeated.

*Sub B1*  
*Cont'D*

86. The method of claim 81, wherein the period between administration of the DNA damaging agent and vector is between 12 and 24 hours.

87. The method of claim 81, wherein the period between administration of the DNA damaging agent and vector is between 6 and 12 hours.

88. The method of claim 81, wherein the period between administration of the DNA damaging agent and vector is about 12 hours.

89. The method of claim 80, wherein the period between administration of the vector and DNA damaging agent is between 12 and 24 hours.

90. The method of claim 80, wherein the period between administration of the vector and DNA damaging agent is between 6 and 12 hours.

91. The method of claim 80, wherein the period between administration of the vector and DNA damaging agent is about 12 hours.

*Q6ex*  
92. The method of claim 28, wherein said vector is delivered endoscopically, intravenously, intratracheally, intralesionally, percutaneously or subcutaneously.

*(VB)*  
93. The method of claim 26, wherein said tumor site is a resected tumor bed.

*B1*  
94. The method of claim 27, wherein said administering is repeated.

*sub D*  
95. The method of claim 28, wherein said tumor cell is a lung cancer cell.

*sub D*  
96. The method of claim 28, wherein said tumor cell is an epithelial tumor cell.

*sub C*  
97. The method of claim 95, wherein said lung cancer cell is non-small cell lung carcinoma cell.

*(VB)*  
98. The method of claim 97, wherein said non-small cell lung carcinoma cell is a squamous carcinoma cell.

*B1*  
99. The method of claim 97, wherein said non-small cell lung carcinoma cell is an adenocarcinoma cell.

100. The method of claim 97, wherein said non-small cell lung carcinoma cell is a large-cell undifferentiated carcinoma cell.

Of count  
SUB B1  
CONT'D

101. The method of claim 95, wherein said lung cancer cell is a small cell lung carcinoma cell.

102. The method of claim 28, wherein said tumor cell is a breast cancer cell.

103. The method of claim 27, wherein said cancer is a lung cancer.

104. The method of claim 27, wherein said cancer is an epithelial cancer.

105. The method of claim 103, wherein said lung cancer is a non-small cell lung carcinoma cancer.

106. The method of claim 105, wherein said non-small cell lung carcinoma cancer is a squamous carcinoma cancer.

107. The method of claim 105, wherein said non-small cell lung carcinoma cancer is an adenocarcinoma cancer.

108. The method of claim 105, wherein said non-small cell lung carcinoma cancer is a large-cell undifferentiated carcinoma cancer.

109. The method of claim 103, wherein said lung cancer is a small cell lung carcinoma cancer.

Q8 cont

110. The method of claim 27, wherein said cancer is breast cancer.

111. The method of claim 28, wherein said vector is administered in about 0.1 ml.

112. The method of claim 28, wherein said vector is administered in about 10 ml.

Sub  
B1

113. The method of claim 28, wherein said vector is administered in about 0.1 ml.

114. The method of claim 28, wherein said vector is administered in about 10 ml.

115. The method of claim 52, wherein said cisplatin is administered at 20 mg/m<sup>2</sup>.

116. The method of claim 53, wherein said doxorubicin is administered at 25-75 mg/m<sup>2</sup>.

117. The method of claim 54, wherein said etoposide is administered at 35-50 mg/m<sup>2</sup>.

118. The method of claim 57, wherein said 5-FU is administered at 3-15 mg/kg.

119. The method of claim 47, wherein the x-ray dosage is between 2000 and 6000 roentgens.

Q8 cont.

120. The method of claim 47, wherein the x-ray dosage is between 50 and 200 roentgens.

121. The method of claim 67, wherein said cisplatin is administered at  $20 \text{ mg/m}^2$ .

122. The method of claim 68, wherein said doxorubicin is administered at  $25-75 \text{ mg/m}^2$ .

123. The method of claim 69, wherein said etoposide is administered at  $35-50 \text{ mg/m}^2$ .

124. The method of claim 72, wherein said 5-FU is administered at  $3-15 \text{ mg/kg}$ .

125. The method of claim 62, wherein the x-ray dosage is between 2000 and 6000 roentgens.

126. The method of claim 62, wherein the x-ray dosage is between 50 and 200 roentgens.

127. The method of claim 7, wherein said promoter is a constitutive promoter.

128. The method of claim 127, wherein the promoter is selected from the group consisting of SV40, CMV and RSV.

129. The method of claim 128, wherein the promoter is the CMV IE promoter.

Active

130. The method of claim 129, wherein the vector further comprises a polyadenylation signal.

131. The method of claim 28, wherein said p53-expressing recombinant, non-viral vector  
comprises a p53 expression region positioned under the control of a promoter.

132. The method of claim 131, wherein said promoter is a constitutive promoter.

133. The method of claim 132, wherein said promoter is selected from the group  
consisting of SV40, CMV and RSV.

134. The method of claim 133, wherein the promoter is the CMV IE promoter.

135. The method of claim 134, wherein the vector further comprises a polyadenylation signal.-

#### REMARKS

The active claims in this case are claims 1-135.

The specification has been amended to recite the relationship with the parent case, i.e.,

Serial No. 08/233,002, filed April 25, 1994.